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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,045	02/21/2007	Kouji Matsushima	14875-157US1 C1-A0308P-US	9112

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EXAMINER	
SKELDING, ZACHARY S	
ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
03/17/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/574,045	MATSUSHIMA ET AL.	
	Examiner	Art Unit	
	ZACHARY SKELDING	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-10 and 31-37* is/are pending in the application.

4a) Of the above claim(s) *8-10,32,33,36 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12-28-10 and 2-4-11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and remarks December 28, 2010 are acknowledged.

   Claims 2, 14, 21-30, and 38-48 have been canceled.

   Claims 6 and 8-10 have been amended.

   Claims 8-10 and 31-37 are now pending.

   Claims 31, 34 and 35 are under consideration wherein the elected species of invention is SEQ ID NO: 4.

   Claims 8-10, 32, 33, 36 and 37 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group or species of invention there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the replies filed on January 7, 2010 and April 13, 2010.

2. The prior grounds of rejection can be found in the Office Action mailed June 28,2 010.

   The prior rejection of claims 2, 21-23, 26, 28, 29, 30, 38, 39, 41, 43, 44, 46 and 48 under 35 U.S.C. 102 (a/e) has been withdrawn in view of applicant's claim amendments.

   The prior rejection of claims 14, 21-24, 26, 28-30, 43, 44, 46 and 48 under 35 U.S.C. 112, first paragraph, enablement, has been withdrawn in view of applicant's claim amendments.

   The prior rejection of claims 14, 21-24, 26, 28-30, 43, 44, 46 and 48 are rejected under 35 U.S.C. 112, first paragraph, written description, has been withdrawn in view of applicant's claim amendments.

3. In a prior phone call with applicant's representative, Mr. McQuade around February 2, 2011, he was asked to query applicant to see if they would be interested in making claim amendments to put the claims into condition for allowance. In particular, discussed with applicant's representative amending the claims via examiner's amendment to be limited to claims 34 and 35. However, after consultation with applicant, applicant's representative indicated that applicant would rather continue prosecution rather than amend the claims at this time (February 10, 2011). In preparing the attached Office Action the first step that was taken was to re-read the prior Office Action and consider applicant's amendments and remarks. In this process of carefully reconsidering applicant's arguments pertaining to claims 34 and 35 it was determined that, contrary to the prior phone discussion, the claimed invention remains unpatentable for the reasons put forth below. The examiner apologizes to applicant for any inconvenience in this matter.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 31, 34 and 35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Davis et al. (WO 03/089624) or Davis et al. (7,317,087), respectively, in view of Takao et al. (JP 2004-208583, published July 29, 2004, cited on an IDS) as evidenced by the teachings of the instant specification at page 3, 1st and 2nd paragraphs and Example 17 at pages 54-55 and the Japanese language Machine translation of Takao et al. JP 2004-208583, translated June 18, 2010, pages 1-32, cited herewith), essentially for the reasons of record as put forth in the Office Action mailed June 28, 2010.

Applicant puts forth an argument that 1) in addition to the teachings of the Davis and Takao references, there were many prior art publications describing sequences having homology to elected species of invention and so applicant alleges that choosing to combine the teachings of Davis with Takao, in the context of all of these other prior art teachings, would not have been obvious; 2) there was allegedly no reason to combine the teachings of Davis and Takao as put forth in the prior Office Action and further such a combination would have been unpredictable or not result in the claimed polypeptide; and 3) "even if one would have been motivated to combine the disclosures of Davis and Takao, it would not have been obvious that the result would have been a naturally occurring polypeptide. Polypeptides that occur naturally would have been predicted to be more biologically relevant than artificially produced polypeptides. The present specification describes the surprising identification of a naturally occurring mRNA encoding the polypeptide isoform of SEQ ID NO:4 (see Example 4). Further, the specification discloses that this particular isoform is present in natural killer cells, which are specialized immune cells thought to play a central role in innate immunity (see Background). The identification of SEQ ID NO:4, which is clearly distinct from the polypeptides disclosed in Davis and Takao, and its expression in natural killer cells provide a valuable contribution to the art of medicine."

As to applicant's argument (1), first it is suggested that the relevant question is not why would "one of skill in the art having knowledge of all of these disclosures…have…selected the polypeptides of Davis and Takao as starting points for modification" as applicant states on page 7, 4th paragraph of their remarks but rather do the presence of these prior art teachings somehow rebut the prima facie case of obviousness based on the teachings of Davis in view of Takao as put forth in the prior Office Action, e.g., by leading one of ordinary skill in the art away from modifying the polypeptide of Davis to include the signal sequence taught by Takao?

In contrast to the teachings of Takao, the other prior art teachings applicant points to (WO 01/49728 and WO 03/054152) are not germane to the teachings of Davis. For example the '728 and '152 publications disclose little of substance about the potential role SEQ ID NO: 121 and SEQ ID NO: 1066 (incorrectly identified by applicant as SEQ ID NO: 155), respectively, in immunity. For example, these other prior art publication do not disclose that their proteins have extracellular immunoglobulin-like domains and structural motifs characteristic of immunoreceptor tyrosine inhibitory motif (ITIM) signaling.

Furthermore, in contrast to the disclosures of Davis and Takao, the sequences of the '728 and '152 publications applicant points to are buried among hundreds of other proteins "having hydrophobic domains" (see the '728 publication Abstract) or hundreds of other proteins cloned from cDNAs (see the '152 publication at pages 110-114).

As to the EP 1201681 publication, applicant indicates this is already of record, however a copy of the '681 publication does not appear to be contained in the IFW.

Moreover, as described in applicant's arguments, these other prior art proteins have a great many differences in their sequences that lie throughout the length of the protein compared to claimed SEQ ID NO: 4, and by proxy, the polypeptide of Davis which is nearly identical to SEQ ID NO: 4, but for a seven amino acid N-terminal deletion removing part of the signal sequence.

For example, at page 7, 2nd paragraph of their remarks applicant points to "SEQ ID NO: 155 of WO 03/054152 (already of record), which describes a sequence identical to positions 6 to 364 of claimed SEQ ID NO:4 and also includes an amino-terminal 8-residue sequence not found in SEQ ID NO :4 and a carboxy-terminal 9-residue sequence not found in SEQ ID NO:4."

By contrast, the homology between the polypeptide sequences of Takao and Davis would be readily apparent to one of ordinary skill in the art as shown below:

```
Takao_SIN2          MLPSLGPMLLWTAVLLFVPCVGKTVWLYLQAWPNPVPEGDALTLRCQGWKNTPLSQVKFY 60
Davis_sig+SIN28     -------MLLWTAVLLFVPCVGKTVWLYLQAWPNPVPEGDALTLRCQGWKNTPLSQVKFY 53
                           ************************************************

Takao_SIN2          RDGKFLHFSKENQTLSMGAATVQSRGQYSCSGQVMYIPQTFTQTSETAMVQVQELFPPPV 120
Davis_sig+SIN28     RDGKFLHFSKENQTLSMGAATVQSRGQYSCSGQVMYIPQTFTQTSETAMVQVQELFPPPV 113
                    ************************************************************

Takao_SIN2          LSAIPSPEPREGSLVTLRCQTKLHPLRSALRLLFSFHKDGHTLQDRGPHPELCIPGAKEG 180
Davis_sig+SIN28     LSAIPSPEPREGSLVTLRCQTKLHPLRSALRLLFSFHKDGHTLQDRGPHPELCIPGAKEG 173
                    ************************************************************

Takao_SIN2          DSGLYWCEVAPEGGQVQKQSPQLEVRVQAPVSRPVLTLHHGPADPAVGDMVQLLCEAQRG 240
Davis_sig+SIN28     DSGLYWCEVAPEGGQVQKQSPQLEVRVQAPVSRPVLTLHHGPADPAVGDMVQLLCEAQRG 233
                    ************************************************************

Takao_SIN2          SPPILYSFYLDEKIVGNHSAPCGGTTSLLPFVKSEQDAGNYSCEAENSVSRERSEPPKKLS 300
Davis_sig+SIN28     SPPILYSFYLDEKIVGNHSAPCGGTTSLLPFVKSEQDAGNYSCEAENSVSRERSEPPKKLS 293
                    ************************************************************
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Takao_SIN2          LKGSQVLFTPASNWLVPWLPASLLGLMVIAAALLVYVRSWRKAGPLPSQIPPTAPGGEQC 360
Davis_sig+SIN28     LKGSQVLFTPASNWLVPWLPASLLGLMVIAAALLVYVRSWRKAGPLPSQIPPTAPGGEQC 353
                    ************************************************************

Takao_SIN2          PLYANVHHQKGKDEGVVYSVVHRTSKRGEARSAEPTVGRK---------------------- 400
Davis_sig+SIN28     PLYANVHHQKGKDEGVVYSVVHRTSKRGEARSAEPTVGRKDSSIICAEVKCLQPSEVSST 413
                    ****************************************

Takao_SIN2          ----------------------
Davis_sig+SIN28     EVNMRSRTLQEPLSDCEEVLC 434
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As to applicant's argument (2), the examiner further disagrees because as put forth in the prior Office Action at pages 4-5, both Davis and Takao teach their signal sequences can be used to direct secretion of their respective immunoglobulin-motif and ITIM containing proteins, and given the structural similarities between the Davis and Takao polypeptides one of ordinary skill in the art would have had a reasonable expectation of substituting the signal sequence of Takao for the signal sequence of Davis. In this regard it is noted insofar as one of ordinary skill in the art could have substituted one known element for another, i.e., one signal sequence for another, and the results of such a substitution would have been predictable, i.e., secretion of the polypeptide to which the signal sequence is attached, express suggestion to substitute one equivalent for another need not be present to render such substitution obvious. (see MPEP § 2143).

Furthermore, applicant makes the following argument at page 6, 3rd paragraph of their remarks:

"The Office action asserts that it would have been obvious to extend the signal sequence of Davis with the amino-terminal seven residues of the signal sequence of Takao. However, it is not clear that doing so would have been predicted to result in a functional signal sequence. Alternatively, if one were to simply replace the signal sequence of Davis with that of Takao, the resulting polypeptide sequence would contain a duplication of residues 23 and 24 relative to SEQ ID NO:4."

Applicant's argument is not found convincing for a number of reasons.

First, with respect to one of ordinary skill in the art extending the signal sequence of Davis with the amino-terminal seven residues of the signal sequence of Takao applicant suggests "it is not clear that doing so would have been predicted to result in a functional signal sequence," but provides no sound scientific reasoning or objective evidence in support of their argument. In this regard it is noted that the arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., In re Huang, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). see MPEP § 2145.

Secondly, with respect to applicant's argument that if one were "simply replace" the signal sequence of Davis with that of Takao the resulting polypeptide sequence would contain a duplication of two residues relative to SEQ ID NO:4, this argument is not found convincing

because it fails to properly account for the ordinary creativity of one of ordinary skill in the art.

In particular, the skilled artisan considering the teachings of Davis in view of Takao as put forth in the prior Office Action and above would readily realize that because signal sequence prediction algorithms are generally accurate, i.e., they can identify a typical N-terminal secretion signal, but not always precise, i.e., they do not always predict the precise cleavage point, the signal sequence of Takao should not be literally appended to the mature protein of Davis without accounting for the duplication of residues 23 and 24.

In this regard it is noted that obviousness is viewed through the lens of a person of ordinary skill in the art with consideration of common knowledge and common sense. Dystar Textilfarben GMBH & Co. Deutschland KG v. C.H.Patrick Co., 464 F.3d 1356, 1367, 80 USPQ2d 1641, 1650 (Fed. Cir. 2006). Furthermore, as stated in KSR Int 'l Co. v. Teleflex Inc., 127 S. Ct. 1727, 1742, 82 USPQ2d 1385, 1397 (2007), "[a] person of ordinary skill is also a person of ordinary creativity, not an automaton," and "[a] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." Id.

As to applicant's argument (3), it is not found convincing for a number of reasons.

First, applicant's assertion that a naturally occurring polypeptide "would have been predicted to be more biologically relevant than artificially produced polypeptides" is acknowledged.

However, even if one of ordinary skill in the art arguably would have not recognized the substitution of the signal sequence of Takao for that of Davis would yield a "naturally occurring polypeptide" this alone makes the substitution no less obvious for the reasons put forth in the prior Office Action as described above.

Furthermore, it is not clear why applicant considers disclosure of the claimed polypeptide "surprising" given applicant's assertion at page 6 of their remarks, last sentence that "At the time of filing, various similar polypeptides likely to be additional splice variants were known, other than those of Davis and Takao." Wouldn't the claimed polypeptide be considered just another splice variant by this reasoning?

Moreover, as stated in MPEP § 716.01(c): "Objective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes evidence of unexpected results…arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results…"

Lastly, applicant asserts that "[t]he identification of SEQ ID NO:4, which is clearly distinct from the polypeptides disclosed in Davis and Takao, and its expression in natural killer cells

provide a valuable contribution to the art of medicine." (see page 7, 5th paragraph of applicant's remarks).

Applicant's assertion is acknowledged, however the claims are drawn to SEQ ID NO: 4 and as stated in MPEP § 2112, "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

6. No claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Phuong N. Huynh can be reached on 571-272-0846. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/
Primary Examiner, Art Unit 1644